

When Pigs Fly: A Multidisciplinary Approach to Navigating a Critical Heparin Shortage

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ABSTRACT

A recent outbreak of African swine fever (ASF) in China has claimed the lives of millions of pigs, and although this virus has no health impacts on humans, the disruption of the global pig population has far-reaching negative impacts on economic and pork-derived products, including the creation of the critical drug heparin. The active pharmaceutical ingredient in heparin is derived from pig intestines, and because of the ASF outbreak, the U.S. faces an imminent shortage of heparin. This drug shortage has the potential for profound implications, as heparin is used in a substantial and varied number of medical conditions. In response to notification of the heparin shortage crisis, our institution, Massachusetts General Hospital, activated its Hospital Incident Command System to streamline organization of major stakeholders and

oversee operational and clinical activities required to mitigate the potential risks and optimize alternative effective strategies. This article describes the essential elements of our institution's emergency response plan, including detailed clinical algorithms developed by our experts for maximal heparin conservation and waste reduction by promoting safe and effective alternative strategies. Through this practice, we have also identified opportunities to change providers' prescribing and utilization behaviors for the better. As the ASF has not yet been contained and this crisis continues, the strategies and policies employed by our institution can provide a framework for other institutions to tackle this ongoing challenge and future drug shortage crises. *The Oncologist* 2020;25:334–347

Implications for Practice: A detailed description of how one institution addressed the current heparin crisis, to support heparin conservation and waste reduction, is provided. The strategies used helped decrease heparin use by 80% in less than 2 months of establishing the task force. This accomplishment can be credited to the development of a task force and strategic plan in which experts and stakeholders were quickly identified, offered a part in the decision-making process, and frequently updated. Furthermore, the response system was dynamic, accessible, and one in which challenges were recognized and acted upon. The key to any crisis management is respect for one another and constant and open communication. Heparin is such a widespread drug that this shortage can potentially affect every patient population and provider. Understanding one's institutional needs and the effect of this crisis on those needs is one of the first steps when developing a strategic plan. Continually evaluating and adjusting that approach in response to the needs of the institution are critical to its success. Moreover, as it did for the authors' institution, a constant appraisal of the strategies can lead to opportunities for improvements in organization and practice that can be sustained well beyond the crisis.

INTRODUCTION

On July 30, 2019, members of the U.S. House Committee on Energy and Commerce sent a letter to the Acting Commissioner of the Food and Drug Administration (FDA) questioning the sufficiency of the nation's heparin supply [1]. The authors

of the letter noted that essentially all of the heparin supply in the U.S. is porcine-derived and that approximately 60% of the crude heparin used in the U.S. is imported from China [2]. Because an outbreak of African swine fever (ASF) in China had

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claimed the lives of as many as 150 million of the nation's 440 million pigs in less than 1 year, representatives in the House were significantly concerned about the future availability of heparin [3]. At the time the letter was sent, two companies, Baxter International Inc. and Pfizer Inc.'s Hospira, were already listed on the FDA's website as having shortages of heparin that dated back to as early as November 2017 [4]. Another major manufacturer, a subsidiary of Germany's Fresenius SE, had also started limiting allocations of the drug "due to a potential shortage of raw ingredient" for an "unknown period." With the ASF outbreak ongoing in China and with insufficient reassurance about product availability from U.S. manufacturers and distributors, pharmacists and hospital leaders across the country became increasingly alarmed about their future access to heparin [5, 6].

Drug shortages are not new phenomena for hospitals; however, they are frequently disruptive [7]. In a recent national survey from a health care performance improvement company, 100% of facilities reported being affected by drug shortages, and hospitals were estimated to have spent an additional 8.6 million personnel hours costing an additional \$360 million each year managing the impacts of shortages [8]. Differing drug shortages, however, threaten hospitals in different ways, and the current potential heparin shortage is profoundly concerning for the breadth of health care services it affects. As noted in a letter from the American Society of Hematology (ASH) to the FDA, heparin is used "to treat blood clots..., used prior to surgical procedures to reduce the risks of blood clots [and also] as a polytherapeutic therapy for overdoses, kidney dialysis, open heart surgery, and angina" [9], among several other clinical indications. Moreover, for a variety of patients and types of medical procedures, the implications of not having access to heparin may be life-threatening because therapeutically equivalent alternatives are lacking. Although Congress, the ASH, the American Society of Health-System Pharmacists (ASHP), and other health care advocacy groups have continued to reach out to the FDA, manufacturers, and distributors, institutions and other organizations have been left to struggle with how best to manage their response to the current heparin shortage.

When major drug shortages affect a wide variety of clinical service lines (such as hematology, cardiac surgery, cardiology, nephrology, oncology, and others) and patient conditions, our hospital has previously activated its Emergency Operations Plan (EOP) to respond. The EOP uses the Hospital Incident Command System (HICS) to organize and govern the large number of clinical decisions, communications, supply chain management, and other activities required to effectively mitigate the risks caused by major drug shortages and to maximize the effectiveness of our response. We describe the essential elements of our hospital's emergency response to the current heparin shortage using HICS, as well as offer clinical algorithms developed by our subject matter experts to maximally preserve our heparin supply by identifying safe and effective conservation and alternative strategies.

OPERATIONS

As with other recent complex drug and medical product shortages, such as the intravenous fluid and opioid shortages in

2017–2018 and intravenous immunoglobulin in 2019, our institution's utilization of the HICS framework allows our hospital to provide a modular response to drug shortages that is scalable to meet current and future impacts. The response to the heparin shortage required multifaceted considerations, as the impacts transcend beyond bedside patient care. From inventory logistics and modification to clinical practices, to ensuring frequent communications, the complexity of medication shortages on hospitals cannot be overstated.

HICS utilizes nationally recognized incident management principles and functional areas to help establish response support, identify problems, and provide a unified multidisciplinary support structure [10, 11]. Subject matter experts at Massachusetts General Hospital (MGH) were asked to fill the key HICS roles (Fig. 1), called Section Chiefs, to support different aspects of the response. Point individuals from providers, pharmacy, nursing, patient safety, finance, and emergency preparedness filled the remaining positions.

To understand and support the daily operations for heparin use, a "Service Lead" model was established to identify and implement any practice changes. The Service Leads were made up of physician, nursing, and pharmacy representation from areas most affected by the heparin shortage, which included perioperative services, cardiology, cardiac surgery, neurology, hematology, oncology, and pediatrics. Roughly 30 services were represented across 120 individuals at MGH. The Service Leads met frequently to develop and coordinate response efforts. This model allowed stakeholders to have a voice and be part of the decision-making process at every step and was a venue through which they could bring up challenges. The Service Leads provided expert guidance on alternative anticoagulation therapy recommendations and strategies to conserve heparin supplies.

At the height of the shortage, as HICS leaders asked clinicians to make needed operational changes to their use of medications, accurate information sharing was paramount to drive accountability, consistency, and trust. To develop a single source of information, a dedicated "intranet" site was developed to facilitate real-time sharing of updates and serve as a reference library for clinical guidance documents. Staff were advised to link their online departmental Web pages and other resources to the central HICS documents to ensure any emergent updates or changes that came later were captured. Other messages were embedded right at the source; for example, within our Epic (Epic Systems Corporation, Verona, WI) electronic health record (EHR) system, an alert message was created such that a provider could not order a heparin product without first acknowledging detailed clinical guidance on the alternatives, with a direct link to additional information on indications and dosing.

Alternative Anticoagulation Therapy for Heparin Conservation

Central to mitigating any drug shortage is resource conservation and waste reduction. To identify opportunities for these actions, our task force and Service Leads proactively evaluated the indication and utilization of all heparin products administered at our institution. Once a list of high-volume and primary indications was identified, a tiered approach to therapy was generated. Indications for which

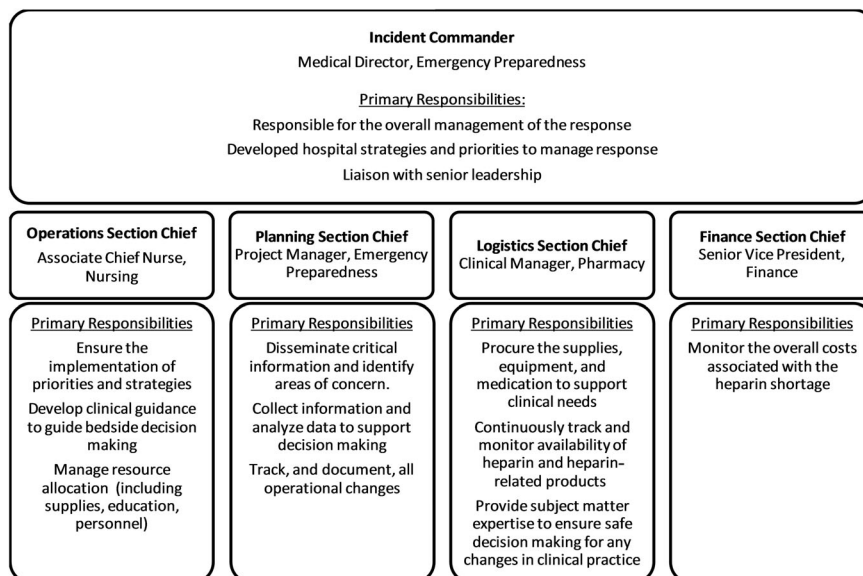


Figure 1. The Massachusetts General Hospital heparin shortage incident command structure.

heparin is a life-sustaining therapy with no acceptable alternatives in regard to both efficacy and safety were assigned Tier A, followed by Tiers B, C, and D (Table 1). Tier D indications were targeted for heparin conservation first, and a workgroup was convened to establish therapeutic alternative recommendations.

The first task undertaken by this workgroup was developing alternative therapy recommendations for treatment and prophylaxis of venous thromboembolism (VTE) in select patient populations, as this indication composed approximately 65% of the heparin product utilization at our institution. At our institution, heparin 5,000 units subcutaneously every 8 hours was standard of care for many of the hospital services. Robust data exist for the efficacy and safety of low molecular weight heparin (LMWH) as an alternative therapy to heparin for VTE prophylaxis, and indeed, multiple society guidelines recommend its use as a first-line agent [12–15]. Limited data exist to support heparin 5,000 units subcutaneously every 8 hours over every 12 hours, with both dosing strategies having grade 1B recommendations from the American College of Chest Physicians [12]. Available literature also supports the use of fondaparinux, apixaban, rivaroxaban, dabigatran, and betrixaban for venous thromboembolism prophylaxis in select patient populations [16–22]. We stratified recommendations based on strength of the literature, patient population served, and available agents on hospital formulary to promote utilization of LMWH therapy and alternative agents as clinically appropriate (Table 2). Therapeutic parenteral anticoagulation alternatives, such as bivalirudin, argatroban, enoxaparin, fondaparinux, and oral anticoagulation alternatives, were also identified and recommended in a stepwise approach based on availability for treatment indications after consultation with specialty provider stakeholders (Table 3). These guidelines were reviewed and approved by a multidisciplinary group of hematologists, pharmacists, provider stakeholders (e.g., neurologists, cardiologists, surgeons), nursing leadership, our Thrombosis Committee, the Service Leads, and finally our Pharmacy Therapeutics Safety Committee.

Table 1. Tiered approach to heparin conservation by indication

Tier	Heparin definition	Example
A	Lifesaving treatment with no therapeutic alternatives	Cardiopulmonary bypass perfusion Acute limb or mesenteric ischemia due to arterial occlusion
B	Essential or preferred treatment with no therapeutic alternatives	Critical carotid stenosis in patients who need urgent endarterectomy Cardiac ablation procedures
C	Lifesaving or essential treatment with acceptable therapeutic alternatives	Acute coronary syndromes
D	May be preferred treatment by specialty, but acceptable therapeutic alternatives exist	Venous thromboembolism prophylaxis Venous thromboembolism treatment Terminal flushing of central lines

Development of the therapeutic and prophylactic anticoagulation alternative therapy guidelines identified true gaps in infrastructure and educational needs. As bivalirudin and argatroban have historically only been administered under close oversight of a hematologist at our institution, widespread use of these agents required enhanced clinician education and guidance. Institutional specific medication guidelines for bivalirudin and argatroban were strengthened to include detailed directions on initial starting dose selection, titration, and monitoring. Widespread dissemination through multidisciplinary education was critical and provided through e-mail and electronic health record clinical alerts, in-person educational conferences, and targeted education at the bedside for each new therapy start. All documents created were considered living documents that were updated continuously as needs for clarification or opportunities for enhanced patient safety arose. Given that dosing regimens may vary between anticoagulant agents (e.g., initial starting rates—bivalirudin 0.15 mg/kg per hour,

Table 2. Recommendations for adult venous thromboembolism chemoprophylaxis during heparin shortage

Patient Population	Order of Preference	VTE prophylaxis	Usual Dose*	May be Used in the Following Patient Populations	Relative Contraindications (Consult Pharmacy if Needed)	Additional Notes
In-patient ambulating, low VTE risk	1	No chemoprophylaxis	N/A	In-patients who are ambulatory and with LOW VTE risk. Please document in EPIC VTE Order Set.	Direct Oral Anticoagulants • Apixaban (CrCl < 15 mL/min) ³³ • Dabigatran (CrCl < 30 mL/min) ³⁵ • Rivaroxaban (CrCl < 30 mL/min) ³¹	Endurals • Refer to neuraxial guidelines for details on dosing and removal of catheter ⁴⁶
	1	Enoxaparin ⁴⁰	40 mg SQ q24h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, ³⁴ low bleed risk	• Potential for invasive procedures	Surgery (ortho) • Dosing for aspirin and warfarin varies among studies. Refer to American College of Chest Physicians guidelines for specifics ³⁷
	2	Rivaroxaban ³¹	10 mg PO q24h	CrCl ≥ 30 mL/min, patients with history of HIT/HITT, low bleed risk	• History of stomach or proximal small intestine surgery	• Warfarin varies among studies. Refer to American College of Chest Physicians guidelines for specifics ³⁷
	3	Fondaparinux ⁴²	2.5 mg SQ q24h	Fluctuating renal function, high bleed risk, potential for invasive procedures	• Dabigatran capsules should not be opened or crushed	• American College of Chest Physicians guidelines for specifics ³⁷
Trauma/ Spinal Cord Injury	1	UFH	5000 units SQ q12h	Fluctuating renal function, high bleed risk, potential for invasive procedures	• Rivaroxaban should not be administered through a jejunostomy tube (J-tube)	
	2	Enoxaparin	40 mg SQ q24h	High VTE risk, stable renal function	• Avoid use in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy [See Supplemental Content 2 (Table S3)]	Cancer • Avoid use of direct oral anticoagulants (e.g., apixaban or rivaroxaban) in patients with gastrointestinal and genitourinary cancer with lesions ^{40,41}
	2	UFH	5000 units SQ q12h	Fluctuating renal function, high bleed risk, potential for invasive procedures	• Major DDIs (rifampin, phenytoin, phenobarbital, carbamazepine, azole antifungals, etc.)	
	3	Fondaparinux	2.5 mg SQ q24h	CrCl ≥ 30 mL/min, patients with history of HIT/HITT, low bleed risk	• Thrombocytopenia (PLT count < 30,000)	
Surgery (Non-Ortho)	1	Enoxaparin	40 mg SQ q24h	No recent bleeding, CrCl ≥ 15 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Within 72 hours of fibrinolysis treatment for acute ischemic stroke	Pregnancy • Reason for prophylaxis: hospitalized for indication other than delivery or if patient on prophylactic anticoagulation in the outpatient setting or antepartum and need for prophylactic anticoagulation
	2	Apixaban ³³	2.5 mg PO q12h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Recent intracranial or gastrointestinal hemorrhage	
	2	Rivaroxaban	10 mg PO q24h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Diagnosis of triple-positive antiphospholipid antibody syndrome	
	3	Fondaparinux	2.5 mg SQ q24h	CrCl ≥ 30 mL/min, patients with history of HIT/HITT, low bleed risk	• Gastrointestinal and genitourinary cancer with active intraluminal lesions	
Surgery (Ortho)	1	Enoxaparin	40 mg SQ q24h	No recent bleeding, CrCl ≥ 15 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Epidural placement	
	1	Apixaban	2.5 mg PO q12h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Apixaban should not be used in this setting based on the ADOPT trial ³⁹	
	1	Dabigatran	110 mg x1, 220 mg q24h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	Enoxaparin⁴⁰ • CrCl < 15 mL/min or fluctuating renal function	
	1	Rivaroxaban	10 mg PO q24h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• History of HIT/HITT	
Cancer ⁴⁴	1	Fondaparinux	2.5 mg SQ q24h	Low-risk for VTE per surgeon discretion based on absence or remote history of select medical co-morbidities	• Allergy to enoxaparin	
	2	Aspirin ⁴⁵	Dose varies ³⁷	High-risk for VTE per surgeon discretion (e.g., hypercoagulable state, morbid obesity, prolonged immobility, history of VTE)	Fondaparinux⁴² • CrCl < 30 mL/min or fluctuating renal function	
	2	Warfarin ⁴⁵	Dose varies ^{37,38}	High-risk for VTE per surgeon discretion (e.g., hypercoagulable state, morbid obesity, prolonged immobility, history of VTE)	• Weight < 50 kg	
	3	UFH	5000 units SQ q12h	Fluctuating renal function, high bleed risk, potential for invasive procedures	• Potential for invasive procedures or high bleed risk	
Pregnancy*	1	Enoxaparin	40 mg SQ q24h	CrCl ≥ 30 mL/min, patients with history of HIT/HITT, low bleed risk	UFH • History of HIT/HITT	
	2	Fondaparinux	2.5 mg SQ q24h	No recent bleeding, CrCl ≥ 15 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk	• Allergy to heparin	
	2	Apixaban	2.5 mg PO q12h	No recent bleeding, CrCl ≥ 30 mL/min, enteral access, no major DDIs, history of HIT/HITT, low bleed risk		
	3	Rivaroxaban	10 mg PO q24h	Fluctuating renal function, high bleed risk, potential for invasive procedures		
Pregnancy*	1	UFH	5000 units SQ q12h	Patients with CrCl < 30 mL/min		
	2	Enoxaparin	40 mg SQ q24h			
	2	UFH	5000 units SQ q12h			
	2	UFH	5000 units SQ q12h			

*See Supplemental Content 2 (Table S1) for dosing in special populations.

Abbreviations: CrCl, creatinine clearance; DDIs, drug-drug interactions; HIT, heparin-induced thrombocytopenia; HITT, Q6 heparin-induced thrombocytopenia thrombosis; ICU, intensive care unit; N/A, not applicable; ortho, orthopedic; PLT, platelet; PO, per os (oral route); q8h, every 8 hours; q12h, every 12 hours; q24h, every 24 hours; SQ, subcutaneous route; UFH, unfractionated heparin; VTE, venous thromboembolism.

Table 3. Recommendations for alternative therapeutic anticoagulation strategies for acute events during heparin shortage

Indication for Anticoagulation	Order of Preference	Alternative Agents	Usual Dose*	Relative or Absolute Contraindications (Consult Pharmacy if Needed)	Additional Notes
Atrial Fibrillation	1	Apixaban	5 mg PO q12h	Direct Acting Oral Anticoagulants • Rivaroxaban and Dabigatran (Contraindicated in CrCl < 30 mL/min for VTE; < 15 mL/min for atrial fibrillation) • Potential for invasive procedures • History of stomach or proximal small intestine surgery • Dabigatran capsules should not be opened or crushed • Rivaroxaban should not be administered through jejunostomy tube (J-tube) • Avoid use in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy • Major Drug-Drug Interactions (rifampin, phenytoin, phenobarbital, carbamazepine, azole antifungals, etc.) [See Supplemental Content 2 (Table S2)] • Thrombocytopenia (PLT count < 30,000) • Diagnosis of triple-positive antiphospholipid antibody syndrome • There are limited clinical data available for patients at the extreme of weight (see Supplemental Content 2) ³⁵⁻³⁷ • Gastrointestinal and genitourinary cancer with active intraluminal lesions • Epidural placement	Non-valvular Atrial Fibrillation • Consult hematology if moderate to high thrombotic risk and consider bridge therapy with enoxaparin or UFH • STEMI, with or without shock • If there is a STEMI and a short delay to cath lab, may use UFH infusion as primary anticoagulate • IVC Filter (Contraindication to anticoagulation with VTE) • Consider IVC filter placement if unable to anticoagulate • Consult Vascular Medicine or Interventional Radiology • Massive PE or Limb-Threatening VTE • UFH preferred in patients who may potentially receive thrombolysis therapy • Submassive PE high-risk PE • Once clinically stable for 24-48 hours and no procedures planned, consider transition to DOAC if no contraindications • Submassive PE intermediate-risk PE • Once clinically stable for 24-48 hours and no procedures planned, transition to DOAC if no contraindications • Dabigatran, edoxaban ³⁸ and warfarin are therapeutic options for the management of VTE when patients are eligible for oral therapy. During the UFH shortage, alternative oral anticoagulants were preferred to decrease the need for a minimum of 5 days of parenteral therapy to conserve parenteral supplies • DVT or Low-risk PE • Intravenous anticoagulation (argatroban, bivalirudin, or heparin) reserved for patients with high-risk of bleeding, potential for imminent procedure, or contraindications to DOACs, enoxaparin, or fondaparinux • Dabigatran, edoxaban and warfarin are therapeutic options for the management of VTE when patients are eligible for oral therapy. During the UFH shortage, alternative oral anticoagulants were preferred to decrease the need for a minimum of 5 days of parenteral therapy to conserve parenteral supplies
		Dabigatran	150 mg PO q12h		
	2	Rivaroxaban	20 mg PO q24h		
		Warfarin ³⁸	Dose Varies		
Acute Coronary Syndromes	1	Enoxaparin bridge to warfarin	1 mg/kg SQ q12h	Enoxaparin • CrCl < 15 mL/min or fluctuating renal function: Consult pharmacy • History of HIT/HITT • Allergy to enoxaparin Fondaparinux • CrCl < 30 mL/min or fluctuating renal function: Consult pharmacy • Potential for invasive procedures • High bleed risk UFH • History of HIT/HITT • Allergy to heparin	Per Protocol
		UFH bridge to warfarin	Per Protocol		
	1	Heparin bolus + bivalirudin continuous IV infusion	Per Protocol		
		Heparin bolus + bivalirudin continuous IV infusion	Per Protocol		
	1	Enoxaparin	1 mg/kg SQ q12h		
		Bivalirudin ⁴²	Per Protocol		
	2	Enoxaparin	Per Protocol		
		UFH	Per Protocol		
	1	Argatroban ⁴³⁻⁴⁴	Per Protocol		
		Bivalirudin	Per Protocol		
	2	UFH	Per Protocol		
		Argatroban	Per Protocol		
	1	Bivalirudin	Per Protocol		
		UFH	Per Protocol		
	2	Enoxaparin	Per Protocol		
		Argatroban	Per Protocol		
VTE ³⁹	1	Bivalirudin	Per Protocol		
		UFH	Per Protocol		
	2	Enoxaparin	1 mg/kg SQ q12h		
		Apixaban	10 mg PO q12h x 7 days followed by 5 mg PO q12h		
	3	Rivaroxaban	15 mg PO q12h x 21 days followed by 20 mg PO q24h		
		Argatroban	Per Protocol		
	4	Bivalirudin	Per Protocol		
		UFH	Per Protocol		
	1	Apixaban	10 mg PO q12h x 7 days followed by 5 mg PO q12h		
		Rivaroxaban	15 mg PO q12h x 21 days followed by 20 mg PO q24h		
	2	Enoxaparin	1 mg/kg SQ q12h		
		Fondaparinux	< 50 kg: 5 mg SQ q24h 50 - 100 kg: 7.5 mg SQ q24h >100 kg: 10 mg SQ q24h		
	3	Argatroban	Per Protocol		
		Bivalirudin	Per Protocol		
	4	UFH	Per Protocol		
		Bivalirudin	Per Protocol		
ECMO	1	Bivalirudin	Per Protocol		
		UFH	Per Protocol		
	2	UFH	Per Protocol		
		UFH	Per Protocol		
	1	IVC Filter ⁴⁰	N/A		
		Enoxaparin	1 mg/kg SQ q12h		
Planned surgical procedure	2	UFH	Per Protocol		

(continued)

Table 3. (continued)

	Cancer ^e	1	Enoxaparin Apixaban ^g (see note) Rivaroxaban ^h (see note) Fondaparinux	1 mg/kg SQ q12h 10 mg PO q12h x 7 days followed by 5 mg PO q12h 15 mg PO q12h x 21 days followed by 20 mg PO q24h < 50 kg: 5 mg SQ q24h 50 - 100 kg: 7.5 mg SQ q24h >100 kg: 10 mg SQ q24h Per Protocol (Use in patients with renal failure)		
ATE	ATE (e.g., limb ischemia or mesenteric ischemia) <i>Excludes ischemic strokes and ACS</i>	1	UFH	Per Protocol		
		2	Enoxaparin ^h	1 mg/kg SQ q12h Per Protocol		
Mechanical Circulatory Support	Mechanical Circulatory Support (e.g., VAD, IABP)	1	Bivalirudin	Per Protocol		
		2	UFH	Per Protocol		

^e **Cancer**
 • **NOTE:** These algorithms are designed for inpatient use only. In our institution, during this current heparin shortage, the majority of cancer patients with VTE are treated with LMWH while hospitalized. This practice is due to a number of reasons such as the need for procedures or acute medical issues where a parenteral, short acting, and easily reversible agent is preferred. The use of DOACs in patients with cancer and VTE has recently been explored, and therefore, their use can be considered after carefully balancing the risks of recurrent VTE with the risks of bleeding in patients who are eligible for oral therapy.⁴⁹⁻⁵¹
 • Edoxaban⁵¹ is a therapeutic option for the management of VTE when patients are eligible for oral therapy and after carefully reviewing the risks of recurrent VTE versus bleeding. During the UFH shortage, alternative oral anticoagulants were preferred to decrease the need for a minimum of 5 days of parenteral therapy to conserve parenteral supplies.
 • Avoid use of DOACs in patients with gastrointestinal and genitourinary cancer with active intraluminal lesions.⁴⁹⁻⁵¹
^h **Enoxaparin and Arterial Thromboembolism**
 • Initiate therapy with UFH and transition to enoxaparin if surgery is not indicated or once hemostasis achieved post-surgery and no contraindications to enoxaparin

*See Supplemental Tables S2 and S3 for dosing in special populations.

Abbreviations: ACS, acute coronary syndromes; ATE, arterial thromboembolism; CrCl, creatinine clearance; DTI, direct thrombin inhibitor; DOAC, direct acting oral anticoagulant; DVT, deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; HIT, heparin-induced thrombocytopenia; IABP, intra-aortic balloon pump; IV, intravenous; IVC, inferior vena cava; N/A, not applicable; NSTEMI, non-ST-segment elevation myocardial infarction; PE, pulmonary embolism; PLT, platelet; PO, per os (oral route); q12h, every 12 hours; q24h, every 24 hours; SQ, subcutaneous route; STEMI, ST-segment elevation myocardial infarction; UFH, unfractionated heparin; VAD, ventricular assist device; VTE, venous thromboembolism.

argatroban 1 µg/kg per minute, heparin 18 unit/kg per hour), opportunity for human error was identified within our prescribing and pump programming practices. This safety concern led to implementation of an independent double check procedure, in which providers and nursing staff required an independent verification of dose and rate in the smart infusion pumps prior to administration. Continuous quality improvement and quality assurance evaluation was required to ensure optimal patient efficacy and safety standards in high-risk medications.

Another area for conservation and waste reduction identified was the adjustment of standard processes for patient care planning. Multidisciplinary rounding typically occurs once or twice a day on various units throughout the hospital. During multidisciplinary rounding, anticoagulation therapy plans are often discussed—including indication for therapy, therapy selection, discussion of complications, and in the case of intravenous heparin, transition from intravenous therapy to more patient-convenient subcutaneous or oral therapy. Adjusting timing of discussions for transitioning from intravenous (IV) therapy to align with timing of when a current heparin bag's contents would be fully administered allowed for reduction in waste or excess utilization when alternative therapies were appropriate. For example, if a patient was administered a heparin 100 unit/mL, 250 mL solution at a rate of 12.6 mL per hour, each heparin bag was expected to last approximately 20 hours. If the patient was due for a new bag to be administered at 7:00 a.m. and deemed safe for transition to therapeutic subcutaneous enoxaparin 1 mg/kg every 12 hours, transitioning before multidisciplinary rounds rather than during multidisciplinary rounds might prevent partial utilization of a heparin bag and conserve supplies.

We also minimized heparin waste during cardiac surgery, particularly during transcatheter aortic valve replacement procedures and cardiopulmonary bypass, by “right sizing” the vials from which we drew heparin. Perfusion providers are now responsible for drawing up all heparin doses to be administered. For example, a 1,000 unit/mL, 30 mL vial, with dose calculated from a heparin dose response curve, is utilized for the loading dose, and the remainder of the vial is reserved for the flush solution and initial maintenance of heparin. When the 30 mL vial is depleted, we transition to a 1,000 unit/mL, 10 mL vial for the subsequent dose(s) and/or 1,000 unit/mL, 1 mL vials if we feel that we will not be able to use all 10,000 units in the 10 mL vial. These practices allowed for minimal waste.

Another opportunity for resource conservation within the cardiac areas was reevaluation of our anticoagulation periprocedural bridging practices. An examination of our data showed that many patients with a low or moderate thrombosis risk, as defined by most recent guidelines [23], would typically be bridged with continuous infusion heparin therapy. Transitioning to a risk-stratified bridging approach reduced heparin utilization in low-risk patients. We leveraged our multidisciplinary service lead model to promote best practices including focused education and appropriate bridging pathways posted on our shortage website. Additionally, clinical pharmacists were tasked with intervening on all continuous infusion heparin orders and reached out to providers to discuss best practice if continuous infusion heparin was ordered unnecessarily.

Addressing our practice of using heparin flushes was another area of opportunity to optimize resource conservation. This work began prior to the shortage with an institutional policy update in December 2018 promoting the use of normal saline flushes over heparin flushes for central venous access devices (CVADs); however, in some patient populations the use of heparin flushes persisted. Prior to the shortage, our institutional Materials Management group purchased and distributed flushes, making them readily available for use compared with stocking them in an automated dispensing cabinet. The usage analytics identified inconsistencies in the ordering and documentation of administration with the heparin flushes. Although a number of heparin flushes were available on the various floors, the most utilized was the 100 unit/mL, 5 mL flush. Given that this flush had the potential to be repurposed for compounding other heparin products if supply drastically diminished, we decided to use the heparin shortage as an opportunity to reinforce the use of normal saline as best practice for routine flushing. We also used this as an opportunity to review the evidence and update our policies to include saline flushes as the default flush for CVADs not in use as well as for terminal flushes for CVADs. To facilitate these updated practices, the Quality and Safety arm of the task force created practice alerts sent out by e-mail and posted in the medication rooms that contained a QR code to videos showing the appropriate technique for flushing catheters. Corresponding updates were also made to our EHR to default saline as the preferred flush in our flush order sets within our EHR.

By strategically and proactively evaluating all of the indications for therapeutic and prophylactic heparin, our multidisciplinary collaborative approach led to optimal conservation strategies and waste reduction. Engaging stakeholders, including clinical nurses, ordering providers, pharmacists, and clinical and operational leadership, allowed us to identify opportunity areas for process improvement and implementation of best strategies. Support of the Cardiac Surgery and Perfusion Services was instrumental in early adoption, promotion, and sustaining of these practices for cardiac procedures.

Pharmacy Operations

Within the HICS structure, one of the roles of our Pharmacy Department was to coordinate key aspects of the medication purchasing, inventory, preparation, distribution, and regulatory processes. Our Pharmacy Department followed the guidance outlined by the ASHP guidelines for managing drug product shortages [24]. We identified key internal pharmacy team leads to support the many clinical and operational efforts (Table 4). Evaluation of all pharmacy operations required for heparin procurement, compounding, and distribution occurred simultaneously to identify the urgency of contingency planning and prevent interruption for patient care at our institution.

Our institution uses a “just-in-time” inventory management strategy that attempts to accurately match demand with supply, thereby minimizing cost of inventory on hand and reducing waste. As part of this inventory strategy, our institution typically keeps 7–10 days of heparin (from all sources) on hand, making us particularly vulnerable when an unexpected shortage occurs. Prior to the heparin shortage, our inventory management and distribution practices were split between

Table 4. Pharmacy drug shortage response roles and responsibilities

Team	Role	Responsibilities
Drug Shortage Point Person	Drug Shortage Response Coordinator	Serve as the Logistical Section Chief within the Hospital Incident Command System (HICS) structure Coordinates the entire drug shortage response process within the Department of Pharmacy Maintains open communication with the pharmacy service leads and the HICS Section Chiefs
Supply Chain	Inventory Management Specialist	Ongoing communication with Clinical Managers Daily inventory level and purchase opportunity assessment Follow up regarding questions to purchase alternatives Update inventory and utilization electronic dashboards
	Supply Chain Leadership	Initial assessment of all shortages and clinical impact potential Assess utilization and adjust purchasing strategies Market analysis Interdepartmental communication for storage
Clinical	Clinical Pharmacy Specialist	Clinical decision support Therapeutic drug monitoring Clinician education
	Clinical Pharmacy Leadership	Support clinical staff in providing clinical decision support, dosing, therapeutic monitoring, and clinician education
Operations	Operations Pharmacy Leadership	Develop and implement specialized procedures for storage, preparation, and distribution of shortage item Assess the need for technology and automation changes and facilitate changes in conjunction with informatics, operational, and clinical team members
	Operations Pharmacist	Ensure specialized procedures for storage, preparation, and distribution are maintained Monitor daily appropriate use of shortage item Provide operational support for specialists when needed
	Perioperative Pharmacy Services Leadership	Develop and implement specialized procedures for storage, preparation, and distribution for shortage item in the intraoperative areas Support perioperative staff in providing clinical decision support, dosing, therapeutic monitoring and clinician education
	Perioperative Pharmacist	Ensure specialized procedures for storage, preparation, and distribution of shortage item are maintained Monitor daily appropriate use of shortage item Provide operational support for providers when needed Deliver clinical decision support and clinical education to perioperative staff. Assist with therapeutic drug monitoring
	Hematologist and Pharmacist On-Call	Provide clinical decision support on anticoagulation selection, dosing, and monitoring Approval for off-hour initiation of intravenous continuous anticoagulation (e.g. heparin, argatroban, bivalirudin) for inpatients (excluding periprocedural areas)

Abbreviation: HICS, Hospital Incident Command System.

the Pharmacy Department and our Materials Management services, limiting our ability to have real-time inventory data available across the institution. Our institution used this drug shortage as an opportunity to consolidate heparin product purchasing, storage, and distribution to the Pharmacy Department, turning this crisis into an opportunity to enhance processes, which we will continue even after the resolution of the heparin shortage.

Purchasing

Streamlining our purchasing practices was another opportunity for a systems improvement. Working with their team lead, Pharmacy purchasing personnel reviewed all pathways available to obtain heparin products and their alternatives. Early on, the pharmacy team determined the minimal amount of heparin needed at any given time to ensure continuity of patient care activities and used this amount to serve as a threshold for escalation of mitigation strategies. Inventory was monitored daily by dedicated personnel, and at least twice a week, contact was made with both wholesale suppliers and manufacturers to monitor access to heparin products.

In drug shortage situations, when products become unavailable and are placed on backorder, wholesalers utilize an allocation system to prevent overpurchasing by individual organizations. Allocations can be both protective and beneficial when a product is available to purchase and purchase history matches customer utilization. For example, if an organization purchases 20 units per month of a product, allocations may be set at exactly 20 units per month, and any request to purchase over that amount will be denied by the wholesaler to ensure all wholesaler customers are able to be supported based on historical utilization.

Manufacturer contracts with organizations can pose an additional challenge during medication shortages as manufacturers are beholden to supply their contracted customers first. If another manufacturer experiences a delay, consumers contracted with that manufacturer may seek alternative manufacturers to purchase products. This practice may then perpetuate the drug shortage as the overall supply cannot support the entire market's demand. Individual manufacturers plan production schedules 12–18 months in advance, based on historical market demand and customer contracts. As such, there is limited flexibility for alternate production schedules in the setting of a drug shortage.

With any drug shortage, alternative strategies for conservation and procurement, such as compounding or seeking importation of drugs from outside the U.S., are often considered. As large-volume heparin bags are often used for continuous therapeutic anticoagulation in the treatment of systemic thrombosis, institutional compounding of intravenous solutions from concentrated heparin vials was contemplated as a mitigation strategy during this heparin shortage. Commercially supplied heparin products have expiration dates that exceed 1 year or more from the manufacture date. However, the complex compounding requirements set forth by the U.S. Pharmacopeia (USP) Chapter <797> standards lead to shortened expiration dating (and possibly wasted product), altered storage requirements (e.g., need for refrigeration), and increased labor requirements [5]. Because of these constraints, we reserved institutional compounding to be

implemented as a last resort. As another strategy, questions were raised regarding international availability of porcine or bovine heparin products for importation during the shortage. Purchase of heparin products outside of the U.S. is not available without approval from the U.S. FDA, which is a heavily regulated process. At this time, there are no new products being imported. Increased regulatory constraint and capital investment barriers have resulted in little incentive to build the redundancies necessary for a robust and secure pharmaceutical supply chain [25].

CHALLENGES AND BARRIERS

The ubiquitous use of heparin meant the need for a complex decision-making process, as a single operational change had a downstream impact regarding decisions that could be felt across the institution. Challenges and barriers were experienced at several points in the early response phases that required immediate remediation to ensure safe patient care. During the initial planning efforts, we recognized that the number of stakeholders involved in this shortage was immense. From contingency planning and education, to product allocation and redistribution, it was difficult to ensure all appropriate individuals were identified. To overcome this challenge, heparin utilization data were generated, and members from areas where heparin was heavily utilized were invited to join the task force working group. Our heparin supply is procured for the hospital by multiple departments, including inpatient Materials Management, operating room Materials Management, and Pharmacy. The need to centralize the ordering and distribution of this drug was necessary to allow for improved ability to concisely track product availability, procurement, distribution, and utilization.

Open communication was essential throughout this process. Given the vast amount of knowledge—clinical, operational, supply chain, and the details of changing updates—it was critical that the team maintain transparency at all times. An important part of the communication process was to identify key leaders to carry the message forward to their colleagues. An early aim of the working group was also to cultivate a diverse group of subject matter experts to disseminate information with an appreciation for how it would apply to colleagues in their areas of practice and to become trusted voices representing their groups.

Once the working group was identified and developed clinical guidelines, the next challenge was to determine how to best disseminate those resources to employees across multiple departments and locations. A successful approach to this problem was to offer each department dedicated educational sessions on the alternative therapies and other mitigation strategies, as it applied to their patient population. Educating the whole community about the changes in resources and the alternative medications recommended was another challenge we faced. For example, if an ordering physician was shifting from using heparin to argatroban, there needed to be collaboration with nursing colleagues to account for the more frequent lab draws and monitoring. It was essential that clinicians felt confident in how to use the alternative medications. Additionally, clinicians needed to be prepared to consistently answer questions from patients and family

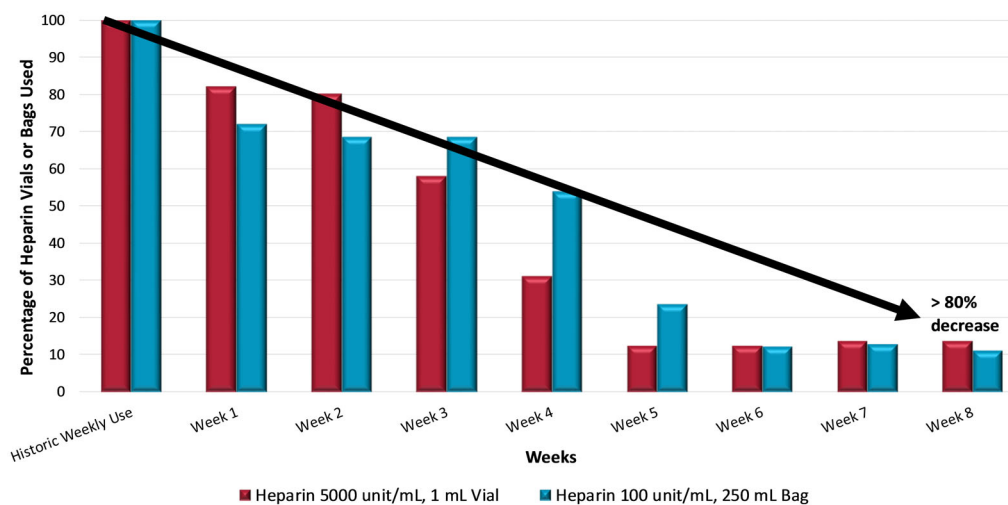


Figure 2. Heparin shortage weekly utilization. Data reflect all inpatient use of heparin products depicted, including operating rooms and procedural areas.

members who had concerns about the shortage and how it was affecting care.

One of the most difficult tasks was communicating to the MGH community the true impact of the shortage. Although some colleagues appreciate the additional information, for others it may be overwhelming. Beyond the clinical guidance, the question in every conference room was “how did this happen?” As is the case with any large-scale crisis, during the initial period of the response there may be multiple messages from multiple sources, some conflicting, which may create confusion and doubt. For the task force, transparency was paramount. The communication plan incorporated information on the supply chain process and details of the entire drug procurement process. Specific time was dedicated to broadening the understanding of the complexity of how global supply networks funnel down to individual facility contracts and ultimately affect bedside care. A number of questions were frequently asked at each Service Lead meeting, such as “How is it that MGH is experiencing a shortage when my colleagues at other institutions have not heard about the heparin shortage?” Ultimately a “frequently asked questions” document was compiled and communicated to help maintain transparency and address these frequently asked questions (supplemental online Content 1). This additional education and communication effort also served to highlight the work of a tremendous team effort including the purchasing group.

RESULTS OF PROCESS IMPLEMENTATION

A transparent communication with proactive engagement of multidisciplinary stakeholders for each specialty area allowed for individualized education dissemination to meet the dynamic needs of each department. Our EHR was leveraged to provide clinical decision support to redirect providers to order alternative therapies unless strict criteria were met. Ensuring buy-in from all stakeholders through the service lead model was central to our success. As all stakeholders were involved in the decision tree for alternative therapy recommendations and understood the urgency of conservation and waste reduction,

rapid practice change was able to efficiently occur. Additionally, this model provided support from multidisciplinary leadership at all levels from ordering providers to department-, division-, and hospital-level leadership. The transparent communication and consideration for cost of alternative therapies allowed for proactive discussion for financial support to accrue adequate supply to meet the needs of our patients.

Overall, this process allowed for a greater than 80% decrease in heparin utilization for our workhorse products (heparin 5,000 unit/mL, 1 mL vial and heparin 100 unit/mL, 250 mL bag) over the course of 45 days (Fig. 2). After implementation of alternative recommendations for VTE chemoprophylaxis (Table 2), heparin composed approximately 16.2% of parenteral chemoprophylaxis therapy compared with 46.5% prior to implementation (Fig. 2). In patients receiving therapeutic anticoagulation, heparin decreased to approximately 24% of parenteral and oral anticoagulation after our strategies were implemented (Table 4; Fig. 3) compared with 35% prior to implementation. We accomplished this in large part by encouraging providers to substitute unfractionated heparin (UFH) with LMWH or a direct oral anticoagulant in appropriate situations. We anecdotally experienced a clinically relevant decrease in the number of patients developing heparin-induced thrombocytopenia (HIT) during the heparin shortage. This is a dramatic difference that can potentially save lives as the mortality associated with HIT can be as high as 40% [26].

Updates with this process allowed for standardization of practices hospitalwide and reevaluation of utilization to ensure best practice standards were being met. Furthermore, this method offered opportunities for enhanced clinician education on all anticoagulation management strategies. Professional staff development was highly encouraged and supported, allowing staff to take on unique leadership roles under the oversight of HICS service leads to support the development of multiple clinical and operational support resources within a short period of time. Involvement of bedside clinicians in all contingency planning discussions allowed for proactive identification of gaps and barriers to address in a strategic manner prior to widespread roll out.

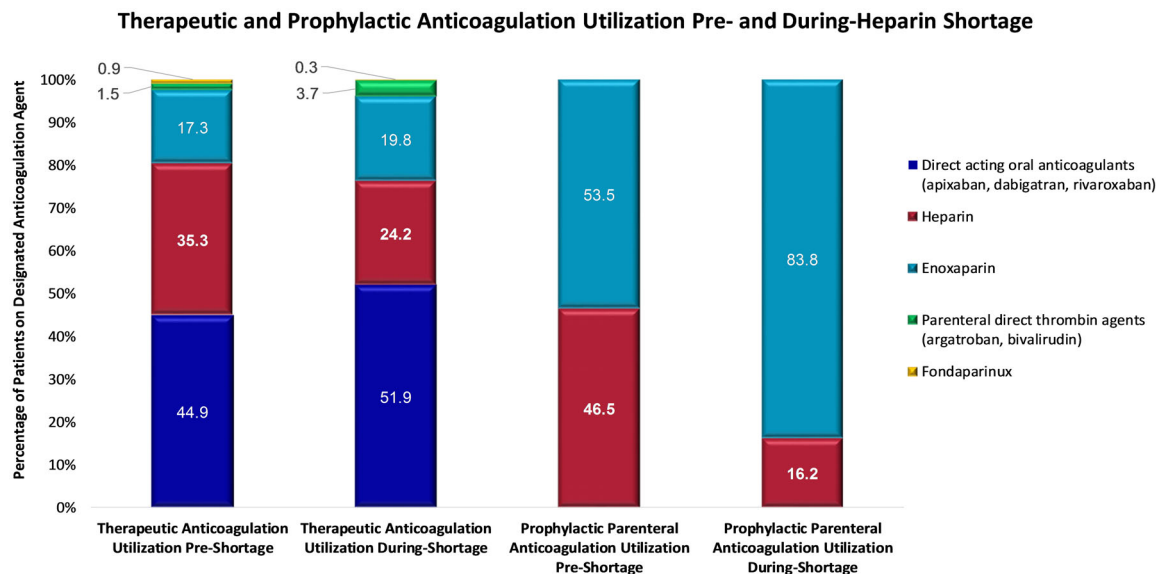


Figure 3. Inpatient therapeutic and prophylactic anticoagulation utilization before and during heparin shortage. Data reflect inpatient units only and exclude operating rooms and procedural areas. Comparison of anticoagulation therapy utilization before shortage (March and April 2019) and during shortage (September and October 2019).

Although this current heparin shortage has certainly been challenging, we have taken a page out of Gupta and colleagues' playbook and used this crisis to thoughtfully examine our current heparin practices and find a silver lining [27]. As Winston Churchill once said, "To improve is to change; to be perfect is to change often" [28]. This crisis has allowed us to look at all our practices around the use of heparin and identify areas that may benefit from a change. For example, LMWH has many advantages over UFH in that it has reliable bioavailability, easier administration, decreased time to therapeutic anticoagulation, and excellent safety profile. Moreover, a recent Cochrane analysis of 29 studies and more than 10,000 patients explored the differences between UFH and LMWH in the initial treatment of venous thromboembolism and found that fixed dose low molecular weight heparin reduced the incidence of recurrent thrombotic complications and occurrence of major hemorrhage during initial treatment compared with unfractionated heparin [29]. We will continue to encourage the use of LMWH even after the crisis given these substantial gains.

This crisis has also provided a platform to promote evidence-based best practices in the use of anticoagulation for periprocedural bridging and agents for flushing vascular access devices, which in turn have allowed for a reduction in heparin use and a better stewardship of resources. Additionally, implications of the ordering and distribution of heparin institutionwide by centralizing supply to pharmacy allowed for increased tracking of administration and distribution data. This shortage has allowed for standardization of treatment practices across the institution and within specific services such as cardiac surgery, vascular surgery, and neurology. Once the heparin shortage subsides, we intend to maintain all waste reduction strategies. Using this crisis to identify areas of change that can potentially improve patient care and outcomes is a benefit that we did not anticipate from the drug shortage, but one that we welcome and will continue to cultivate even after the shortage resolves.

DISCUSSION

Hospitals in the U.S. are facing shortages of essential medications with increasing frequency. Although some drug shortages have relatively less severe clinical impacts on health care operations and patients because of the existence of approximately equivalent alternative therapies, in the past 3 years, hospitals have faced major shortages of essential medications, such as IV opiates, IV immunoglobulin, and now heparin, for which, in certain circumstances, there are no equally effective and safe substitutions. Moreover, the complex clinical indications for use of these indispensable medications extend widely across the many medical specialties within the house of medicine, making it difficult for hospital leaders to compare and prioritize differing clinical practices and patient populations in need.

By utilizing the hospital's EOP and its associated infrastructure to manage the most severe medication shortages, hospitals can both explicitly recognize the gravity of the impacts of these shortages and also develop fair, appropriate, effective, and comprehensive responses to these events. In a disaster, when a hospital is faced with loss of an essential service such as electricity, hospitals activate their EOP and rapidly assemble technical experts and hospital leaders to identify the best ways to respond to the crisis. Similarly, when faced with shortages of medications that are essential for safe patient care, hospitals should also consider utilizing these systems in response. Supply chain expert engagement allows for streamlined procurement and inventory management. Technical experts from all affected clinical services can gather to jointly identify all the uses of the medication within the hospital. These convened experts review patient conditions for which the medication is essential and for which there are no equivalently safe alternative therapies. They can also identify conservation and substitution strategies that may help to mitigate the impact of the shortage. By utilizing

subject matter experts to develop common alternative therapeutic strategies with participation from all affected services and leveraging existing Emergency Management and Quality and Safety teams in the hospital, hospitals can significantly improve the safety and consistency of adoption of these strategies among all providers.

One key element of any hospital's EOP is the development of a communication strategy. With drug shortages, it is vitally important that all affected providers and patients understand the nature of the shortage, the anticipated duration and impacts of the shortage, and the actions being taken in response. By including the hospital's public affairs and communications experts in the response, hospital leaders can ensure that the materials developed are appropriate and clear and that they reach their target audiences effectively. Moreover, by including Service Lead physicians, nurses, pharmacists, and other representatives in the HICS teams managing the hospital response to critical shortages, hospitals can ensure both that the central hospital messaging is effectively delivered to each clinical service and also that any concerns or questions that arise from clinicians within each service have a conduit and an advocate who can communicate those concerns quickly to the central leadership team.

The nature of hospital emergency operations is also iterative, and typical EOPs call for recurring meetings to reassess the evolving nature of each incident and the effectiveness of the institutional response. By utilizing their EOPs, hospitals can monitor the success of their interventions and determine whether additional actions are necessary. Hospitals must regularly communicate updated information regarding the ongoing need for the response strategies as well as data on the effectiveness of mitigation strategies in order to sustain patient and clinician buy-in to the response, especially for protracted shortages.

One of the possible benefits of a drug crisis that may not be apparent initially is the opportunity to recognize areas of change that can have a positive impact on patient care and outcomes. Using LMWH instead of UFH in appropriate situations and using saline instead of heparin to flush catheters are two examples of how we used this crisis as a conduit to change behaviors that promote evidence-based best practices. Through ongoing education and positive feedback to providers, we aim to continue encouraging and reinforcing these enhanced approaches and are open to discovering others.

CONCLUSION

Heparin is an essential medication for several clinical conditions. Indeed, certain procedures, such as cardiac surgery, cannot be done safely without heparin. When the African swine fever affected China's pig population, which is where most of the crude heparin is derived, the supply of heparin to the U.S. became threatened. In response to this drug shortage, our institution activated its Emergency Operations Plan and used our Hospital Incident Command System to create a structure that quickly and efficiently organized all stakeholders, identified problems, and provided a unified multidisciplinary support structure to address the complex clinical decisions, provide transparent and frequent communications, and carry out all activities required to mitigate

the risks and maximize the effectiveness of our response. Moreover, we have taken advantage of this crisis to thoroughly examine our current heparin practices and identify areas in which alternative strategies are more effective and safer. By implementing these new approaches now, we hope they will continue long after the drug shortage is over.

We believe that our detailed and systematic approach to this crisis can help other hospitals that are facing a similar challenge. Although we are a large tertiary academic hospital with numerous resources and a well-developed emergency management infrastructure, we encourage other hospitals that do not have the same construct to modify our strategies to fit their needs. Hospitals should first identify their resources and support systems that are presently in place to deal with such a crisis. If none exist, using our model and the strategies provided can be a starting point and should be adapted to the specific composition of each institution. In conjunction, evaluating the current heparin usage and the potential requirements for the future will help pinpoint the needs of the organization and can be a good starting point for discussions. We recognize that each institution is unique, and as such, each hospital's emergency response should be adjusted accordingly.

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DISCLAIMER

These algorithms were created by clinical experts for use in inpatients at Massachusetts General Hospital. These algorithms should not replace clinical judgment incorporating patient-specific factors or institutional, national, or international guidelines or practice.

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DISCLOSURES

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See <http://www.TheOncologist.com> for supplemental material available online.

Editor's Note:

This article highlights a growing problem in the United States and abroad: the episodic shortage of essential medicines, devices, masks, and even surgical garments and the need for rapid response teams in our hospitals to create effective strategies in order to maintain a high level of care. Oncologists have had to deal with shortages of drugs (e.g., methotrexate), i.v. solutions, antibiotics, and heparin—all essential to our practice. The situation is even more extreme in low- and middle-income countries, where shortages of essential chemotherapy drugs and opioids are common. No doubt the worldwide concerns with the coronavirus outbreak in China will create an unprecedented demand for masks, antibiotics, screening and isolation strategies in our hospitals, and dedicated medical response teams. And, as in other recent shortages and emergent issues, the cancer population is often most at risk when such emergencies occur. We hope to address these emergent needs with relevant articles on how best to respond, and to publish these articles as rapidly as possible.

Editor's Note:

See the related article, “Drug Shortages: The View Across an Ocean” by Andrew Shuman and Yoram Unguru on page 274 of this issue.